PATENT COOPERATION TREATY

From the:
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

21 OCT 2004

PCT

NOTIFICATION OF TRANSMITTAL OF INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Rule 71.1)

To:

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BRISBANE

Date of mailing *day/month/year*	- 3 AUG 2004
Applicant's or agent's file reference 12176212/VPA	IMPORTANT NOTIFICATION

International Application No.	International Filing Date	Priority Date
PCT/AU2003/000454	16 April 2003	22 April 2002

Applicant
QUEENSLAND UNIVERSITY OF TECHNOLOGY et al

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.

2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.

3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translations to those Offices.

4. **REMINDER**

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices)(Article 39(1))(see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide

Name and mailing address of the IPEA/AU	Authorized officer
AUSTRALIAN PATENT OFFICE PO BOX 200, WODEN ACT 2606, AUSTRALIA E-mail address: pct@ipaustralia.gov.au Facsimile No. (02) 6285 3929	ALISTAIR BESTOW Telephone No. (02) 6283 2450

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 12176212/VPA	**FOR FURTHER ACTION**	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416).
International Application No. **PCT/AU2003/000454**	International Filing Date *(day/month/year)* 16 April 2003	Priority Date *(day/month/year)* 22 April 2002
International Patent Classification (IPC) or national classification and IPC **Int. Cl.**[7] G01N 33/574, C12N 15/12, C12Q 1/25		
Applicant QUEENSLAND UNIVERSITY OF TECHNOLOGY et al		

This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 5 sheets, including this cover sheet.

☐ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of sheet(s).

3. This report contains indications relating to the following items:

I	☒	Basis of the report
II	☐	Priority
III	☐	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
IV	☐	Lack of unity of invention
V	☒	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
VI	☐	Certain documents cited
VII	☐	Certain defects in the international application
VIII	☒	Certain observations on the international application

Date of submission of the demand	Date of completion of the report
10 November 2003	27 July 2004
Name and mailing address of the IPEA/AU AUSTRALIAN PATENT OFFICE PO BOX 200, WODEN ACT 2606, AUSTRALIA E-mail address: pct@ipaustralia.gov.au Facsimile No. (02) 6285 3929	Authorized Officer **ALISTAIR BESTOW** Telephone No. (02) 6283 2450

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/AU2003/000454

I. Basis of the report

1. With regard to the **elements** of the international application:*

[X] the international application as originally filed.

[ ] the description, pages , as originally filed,
pages , filed with the demand,
pages , received on with the letter of

[ ] the claims, pages , as originally filed,
pages , as amended (together with any statement) under Article 19,
pages , filed with the demand,
pages , received on with the letter of

[ ] the drawings, pages , as originally filed,
pages , filed with the demand,
pages , received on with the letter of

[ ] the sequence listing part of the description:
pages , as originally filed
pages , filed with the demand
pages , received on with the letter of

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.
These elements were available or furnished to this Authority in the following language which is:

[ ] the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).

[ ] the language of publication of the international application (under Rule 48.3(b)).

[ ] the language of the translation furnished for the purposes of international preliminary examination (under Rules 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

[ ] contained in the international application in written form.

[ ] filed together with the international application in computer readable form.

[ ] furnished subsequently to this Authority in written form.

[ ] furnished subsequently to this Authority in computer readable form.

[ ] The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

[ ] The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

4. [ ] The amendments have resulted in the cancellation of:

[ ] the description, pages

[ ] the claims, Nos.

[ ] the drawings, sheets/fig.

5. [ ] This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).**

* *Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).*

** *Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report*

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	**2, 4-7, 11-13, 15-18, 21-23, 43, 45**	**YES**
	Claims	**1, 3, 8-10, 14, 19-20, 24-42, 44, 46-57**	**NO**
Inventive step (IS)	Claims	**2, 4-7, 11-13, 15-18, 21-23, 43, 45**	**YES**
	Claims	**1, 3, 8-10, 14, 19-20, 24-42, 44, 46-57**	**NO**
Industrial applicability (IA)	Claims	**1 - 57**	**YES**
	Claims		**NO**

2. Citations and explanations (Rule 70.7)

The following documents identified in the International Search Report have been considered for the purposes of this report:

D1 - **http://cis.nci.nih.gov/fact/5_29.htm**

D2 - *Clinical Chemistry and Laboratory Medicine* 1998 36(9):671-81

D3 - WO, A, 2000/049158

D4 - WO, A, 1996/034964

D5 - *Journal of Clinical Oncology* March 2000 18(5):1036-42

D6 - *Journal of Molecular Diagnostics*, 3(3) August 2001:111-22

D7 - http://www.cgen.com/news/press/press130202a.htm

D8 - WO, A, 1999/064594

Extra citations:

D9 - Eur. J. Biochem., vol. 268, 2001, Heuze-Vourc'h et al., pp4408-13

D10 - Mol. Cell. Endocrinol., vol. 76(1-3), 1991, Riegman et al., pp181-90

The present invention would appear to be based on the observation that that certain aberrant PSA and KLK2 transcripts are increased in cancer tissues by comparison with certain benign tissues (see page 2, lines 4-8 of the specification). The specification acknowledges that the aberrant transcripts were, in fact, known (see page 18, lines 17 and 21 and page 19, line 1). Thus, in relation to the inventive concept described by the specification, the relevant question is whether the known aberrant transcripts were known to be associated with prostate cancer.

NOVELTY (N) and INVENTIVE STEP (IS)

Each of D1, D2, D5, D6 and D8 teach that PSA and/or KLK2 were known cancer markers. However, none of these documents would appear to disclose the expression of aberrant forms of the proteins. Therefore, the claims are novel and involve an inventive step in light of D1, D2, D5, D6 and D8.

D3 discloses 'aberrant' transcripts of PSA and KLK2 and teaches that they have utility in the diagnosis and treatment of prostate cancer. See; page 11, lines 6-19; page 13, line 10; page 13, line 21-page 15, line 4. In light of D3, claims 1, 3, 8-10, 14, 19-20, 24-42, 44, and 46-57 are not novel and do not involve an inventive step.

(continued ...)

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

A reading of the specification as a whole indicates that the invention relates to the observation that certain, aberrant, PSA and KLK2 transcripts are associated with prostate cancer. The basis for the assertion of this relationship would appear to be limited to the following passages in the specification:

a) page 2, lines 4-8;

b) page 18, lines 4-7;

c) page 44, lines 22-24 (and Figure 3); and,

d) page 45, lines 20-25 (and Figures 4 and 5).

Passage a) expressly notes that, with respect to PSA RP2 transcript 1, the relationship is only a mere possibility.

The disclosure of passage c), and Figure 3 in particular, is not considered to support the assertion that there exists a relationship between the transcripts and cancer. Figure 3 fails to demonstrate a statistically significant difference between the RP2 transcripts and wild-type expression. Moreover, Figure 3 appears to indicate that the 10A transcript is, in fact, found in all individuals.

Passage d) is the only passage considered capable of supporting the existence of a relationship between the RP2 transcript 2 and KLK2 10A transcripts and cancer. This passage is not considered to support the existence of any such relationship between other transcripts and cancer.

Thus, the entirety of the invention relates to the observation that two particular (previously known) alternative transcripts are associated with cancer. The specification is not capable of supporting claims involving a relationship between any and all aberrant transcripts associated with prostate cancer. That is, only those claims limited to RP2 transcript 2 and KLK2 10A are considered to be supported by the description.

The specification fails to exemplify:

- detection of the protein products of RP2 transcript 2 or KLK2 10A;
- detection of the "functional activity" of the aberrant polypeptides (page 18, line 29 indicates that the aberrant polypeptides are devoid of activity);
- detection of the "functional activity" of a transcript;

  detection of activity or product from tissue other than prostate tissue;
- use of a portion of the expression product (production of the expression product is not exemplified);
- production of antigen-binding molecules (specific or otherwise) to the aberrant products;
- production of ribozymes or RNAi-mediating molecules;
- production of antigen-presenting cells expressing processed form of the aberrant polypeptides; or,
- methods of treatment or prophylaxis.

Claims embodying such methods are not considered fully supported by the description.

Claims 52, 55 and 56 encompass the use of antibodies that are cross reactive with normal PSA or KLK2. As the antigen-binding molecules of these claims are not 'specific' to the aberrant proteins of the invention, these claims are not limited by the characteristic features of the invention.

Supplemental Box
(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of V

D4 discloses 'aberrant' KLK2 variants and teaches that they have utility in the diagnosis of prostate cancer. See page 7, lines 19-25; page 8, lines 8-12; page 13, lines10-14. In light of D4, claims 1, 3, 8-10, 14, 19-20, 24-42, 44, and 46-57 are not novel and do not involve an inventive step.

D7 discloses the existence of splice variants of PSA and teaches that they may provide additional tumour markers for the development of diagnostic tests. However, D7 does not constitute a sufficient disclosure to destroy the novelty or inventive step of the present claims.

D9 and D10 disclose the specific 'aberrant' forms of PSA and KLK2 that the present specification discloses as being associated with prostate cancer. Neither D9 nor D10 discloses a specific relationship between the variant forms of PSA and KLK2 and prostate cancer. Therefore, the claims are novel and involve an inventive step in light of D9 and D10.